Chemistry for Coping With Diabetes: Substance Use/Abuse

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Objectives

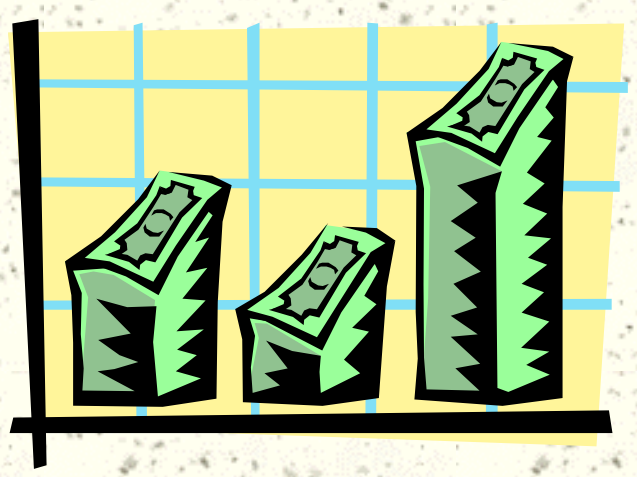
- Describe the epidemiology of substance dependence in the U.S.
- Describe effects of ETOH use in persons with diabetes
- Describe effects of tobacco use in patients with diabetes
- List other substances that may be mis-used and potential adverse consequences
- Discuss relevant drug interactions between diabetes medications and ETOH, tobacco, and other misused substances

Epidemiology of Substance Dependence

- 10-20% of the U.S. population
  - 16 million
- All races, ages, both genders
- Up to 50% of hospitalized patients
- > 100,000 deaths/year are due to alcohol
  - Not MVAs

Cost of Substance Dependence

- $ 67 Billion
  - Health care
  - Drug addiction prevention/treatment programs
  - Drug-related crime



Cost of Substance Dependence

- Costs to society
  - ↓ productivity
  - ↓ ability to function in social situations
  - Death
- Costs to the individual
  - Less able to deal with chronic diseases, such as diabetes
    - Lifestyle issues
    - Medication adherence
    - Monitoring
    - Complications?

What Substances are Used for Chemical Coping?

- ETOH
  - Prevalence of use in the U.S.?
    - 109 million Americans 12 y/o and older
  - Prevalence of use in DM patients?

ETOH Use in Diabetes

- Overuse may impair a person's ability to adhere to appropriate behaviors
  - Take medications
  - Follow appropriate nutrition plan
  - Check blood glucose
  - Recognize hypoglycemia symptoms
  - Recognize hyperglycemia symptoms

ETOH Use in Diabetes

- Overuse of ETOH in anyone may be characterized by
  - Disinhibition of behavioral control centers
  - Impairment of judgment
  - Impairment of cognition
  - Impairment of motor function
  - Risk of suicide
  - Blackouts
    - Consciousness maintained but events for a time period are not recalled

ETOH Use in Diabetes

- ETOH may interact with metformin when a person decides to drink "heavily" or binge drink
  - Lactic acidosis may occur
  - Characterized by acute/intense muscle aches, shortness of breath, difficulty with breathing, palpitations, edema

ETOH Use in Diabetes

- ETOH may interact with secretagogues
  - Disulfiram reactions with first generation sulfonylureas
  - Additive hypoglycemia with secretagogues
    - Sulfonylureas
  - Additive hypoglycemia with insulin

ETOH Use in Diabetes

- Do not drink excessively
- Make one drink last a long time
- Eat carbs at the same time that ETOH is being used
  - Acute ETOH use inhibits hepatic gluconeogenesis
    - The bottom line – hypoglycemia may occur
  - Chronic ETOH use adds calories and should be considered in the meal plan

ETOH Use in Diabetes

- Other issues
  - ETOH may cause additive CNS depression when combined with OTC drugs:
    - OTC sedating antihistamines (diphenhydramine, chlorpheniramine)
    - OTC cough/cold syrups containing ETOH
    - Certain CAM products

ETOH Use in Diabetes

- Other issues
  - ETOH may cause additive CNS depression when combined with prescription drugs:
    - "Muscle relaxants" (Soma, Flexeril)
    - Benzodiazepines (Xanax, Klonopin, Ativan)
    - Opioids (Hydrocodone, codeine, oxycodone)
    - TCAs (amitriptyline, desipramine, imipramine, nortriptyline)
    - MAO inhibitors (hypertensive reaction when alcoholic drink contains tyramine, e.g., tap beers)

ETOH Use in Diabetes

- Other issues
  - When chronic ETOH use is combined with high doses of acetaminophen:
    - Liver toxicity may occur
  - When acute ETOH use is combined with aspirin or NSAIDs:
    - Potential for a GI bleed

ETOH Use in Diabetes

- Other issues
  - "Holiday heart syndrome" may occur on weekends or holidays when heavy drinking or binge drinking occurs
    - Cardiac arrhythmias
  - Binge drinking
    - Ventricular and supraventricular arrhythmias
    - Atrial fibrillation

ETOH Use in Diabetes

- "Holiday heart syndrome" - What is the cause?
  - A hyperadrenergic state occurs (excess of catecholamines)
  - Impaired vagal heart rate control
  - QT interval prolongation
  - Withdrawal may precipitate a hyperadrenergic state

ETOH Use in Diabetes

- A look at long-term consumption and risk of atrial fibrillation (AF) in Framingham patients
- Looked at 1,055 cases of AF during a 50-year follow up
- Logistic regression with adjustment for SBP, baseline age, education, h/o of MI, CHF, DM, LVH, valve heart disease

Djoussé L, et al: Am J Cardiol 2004;93:710-13

ETOH Use in Diabetes

- Results
  - Little risk between long-term moderate consumption and AF
    - RR = 0.97 for 0.1 to 12 gm/day of ETOH
    - RR = 1.06 for 12.1 to 24 gm/day of ETOH
    - RR = 1.12 for 24.1 to 36 gm/day of ETOH
  - Consuming > 3 drinks/day produces a significantly increased risk of AF long-term
    - RR = 1.34 for > 36 gm/day of ETOH

Am J Cardiol 2004;93:710-13.

Is ETOH Use Associated With An Increase In Diabetes?

Is ETOH Use Associated With An Increase in DM-Related Issues?

ETOH and Diabetes

- A systematic review of studies that assessed effect of ETOH on incidence, management, and complications of diabetes
  - 2 assessors reviewed 974 citations
  - 32 articles selected (excluded poor quality studies)
  - Looked at no ETOH, compared to moderate consumption (1-3 drinks/day), and heavy consumption (> 3 drinks/day)

Howard AA et al: Ann Intern Med 2004;140:211-19

ETOH and Diabetes

- For analysis of DM incidence, the outcome was diabetes
- For assessment of glycemic control, outcomes were glucose and HbA1C
- For assessment of self-management behaviors, looked at:
  - Adherence to therapy
  - SMBG
  - MNT
  - Exercise

Howard AA et al: Ann Intern Med 2004;140:211-19

ETOH and Diabetes

- For assessment of medication complications, looked at:
  - Drug serum concentrations
  - ADRs

Howard AA et al: Ann Intern Med 2004;140:211-19

ETOH and Diabetes

- For assessment of acute complications, looked at:
  - DKA
  - Hyperosmolar coma
  - Infection
  - Amputation

Howard AA et al: Ann Intern Med 2004;140:211-19

ETOH and Diabetes

- For assessment of microvascular complications, looked at:
  - Retinopathy
  - Peripheral neuropathy
  - Nephropathy
  - Erectile dysfunction

Howard AA et al: Ann Intern Med 2004;140:211-19

ETOH and Diabetes

- For assessment of macrovascular complications, looked at:
  - Coronary heart disease
  - Cerebrovascular disease
  - Peripheral vascular disease

Howard AA et al: Ann Intern Med 2004;140:211-19

ETOH and Diabetes

- Results for relationship between ETOH use and DM
  - U-shaped curve in 5 studies
    - E.g., moderate drinkers have lowest risk for DM
    - Heavy drinkers and nondrinkers had higher risk
    - 1-3 drinks/day: 33% to 56% ↓ in DM risk
    - > 3 drinks/day: 43% ↑ in DM risk

Howard AA et al: Ann Intern Med 2004;140:211-19

ETOH and Diabetes

- Results for relationship between ETOH use and DM
  - 3 studies found inverse relationship between ETOH use and DM incidence:
    - 43-46% ↓ in risk for DM for moderate ETOH consumption, compared with nondrinkers

Howard AA et al: Ann Intern Med 2004;140:211-19

ETOH and Diabetes

- Results for relationship between ETOH use and glycemic control
  - 2 studies found ↓ in Plasma Glucose after ETOH consumption with/without a meal
  - 3 studies found that small-moderate ETOH amounts with/without food had no acute effect on glycemic control

Howard AA et al: Ann Intern Med 2004;140:211-19

ETOH and Diabetes

- Results for relationship between ETOH use and medication complications
  - 2 studies assessed troglitazone use – no acute problems
  - With chlorpropamide – decreased rate of ETOH elimination from the blood but no adverse outcomes

Howard AA et al: Ann Intern Med 2004;140:211-19

ETOH and Diabetes

- Results for relationship between ETOH use and DM self-care behaviors
  - No studies found
  - However, it may adversely affect these self-care behaviors since ETOH use is associated with nonadherence to medical therapy in other disease states (HIV)

Howard AA et al: Ann Intern Med 2004;140:211-19

ETOH and Diabetes

- Results for relationship between ETOH use and microvascular complications
  - 2 studies assessed risk for retinopathy
    - One study (rated fair) found an ↑ risk for retinopathy with heavy ETOH use
    - One study (rated good) found no association between ETOH use and incidence or progression of retinopathy

Howard AA et al: Ann Intern Med 2004;140:211-19

ETOH and Diabetes

- Results for relationship between ETOH use and macrovascular complications (MI)
  - 2 studies rated "good" and 2 rated "fair"
  - Limitation – ETOH consumption assessed only at baseline
  - Results
    - Moderate drinkers had 34-55% ↓ risk for CHD (compared to nondrinkers)
    - Moderate drinkers had 55-79% ↓ risk for death due to CHD (compared to nondrinkers)

Howard AA et al: Ann Intern Med 2004;140:211-19

ETOH and Diabetes: Summary of Articles Reviewed

- Moderate ETOH consumption is associated with ↓ incidence of DM
- Heavy ETOH use may be associated with ↑ incidence of DM
- No evidence of acute effect of moderate ETOH use on glycemic control
- Effect of ETOH use on self-care behaviors is not well studied

Howard AA et al: Ann Intern Med 2004;140:211-19

ETOH and Diabetes: Summary of Articles Reviewed

- Limited evidence that ETOH use with TZD or sulfonylurea does not cause an ADR (NOT WELL STUDIED!!)
- Strong evidence that moderate ETOH use is associated with ↓ CHD in DM
- Evidence is insufficient to establish effect of ETOH use on noncardiac complications (retinopathy, neuropathy, etc.)

Howard AA et al: Ann Intern Med 2004;140:211-19

What If You Suspect ETOH Overuse – What Clues Are Available?

Clues

- Trauma questions
  - Fractures, injuries
  - MVAs
  - Fights
- Drug testing?

Clues

- CAGE
  - Have you ever felt you ought to **C**ut down on your drinking?
  - Have people **A**nnoyed you by criticizing your drinking?
  - Have you ever felt bad or **G**uilty about your drinking?
  - Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover? (**E**ye opener)?

Clues

- Alcohol Use Disorders Identification Test (AUDIT)
  - 10-item multiple choice "waiting room" type of survey
  - Includes the CAGE questions
  - Other questions assess:
    - Quantity/frequency of ETOH consumption
    - Blackouts
    - Injuries

What Other Substances are Used for Coping?

- Tobacco
  - Prevalence of use in the U.S.
    - 22.5% of adults are current smokers
      - 25.2% male
      - 20% female
    - 81.8% smoke daily
    - 18.2% smoke some days
  - 70% of smokers want to quit

What Other Substances are Used for Coping?

- Tobacco
  - Prevalence of use in different states
    - Kentucky – 32.6%
    - Nevada – 26%
    - Illinois 22.9%
    - Texas 22.9%
    - New York – 22.4%
    - California 16.4%
    - Utah – 12.7%

What Other Substances are Used for Coping?

- Tobacco
  - Prevalence of use in different ethnic groups
    - Native American/Alaskan Native – 40.8%
    - White, Non-Hispanic – 23.6%
    - Black, Non-Hispanic – 22.4%
    - Hispanic – 16.7%
    - Asian/Pacific Islander – 13.3%
  - Prevalence of use in DM patients?

Tobacco

- Everything you need for support of healthcare providers and patients is found at:

www.surgeongeneral.gov/tobacco

Tobacco Use

- Why is tobacco use such a concern?
  - > 400,000 deaths/year in the U.S.
    - Most are PREVENTABLE!
  - > 1,000 deaths/day

Tobacco Use

- Costs of Tobacco Use
  - Medical Expenditures (1998)
    - Ambulatory care - $27.2 billion
    - Hospital care - $17.1 billion
    - Nursing home care - $19.4 billion
    - Prescription drugs - $ 6.4 billion
    - Other care - $ 5.4 billion

Tobacco Use

- Costs of Tobacco Use
  - Lost Productivity costs (1995-99)
    - Men - $55.4 billion
    - Women - $26.5 billion
  - Costs to Society
    - $7.18 per pack

Tobacco Use

- Should be considered a vital sign in all patients:
  - Along with BP, HR, weight, etc…"Do you smoke?"
- Tobacco use has the potential to cause illness
- Tobacco use has the potential to produce drug-disease interactions

Tobacco Use

- What types of problems may occur?
  - Cosmetic
  - Cardiac problems
    - Atherosclerosis
    - CHD
    - Stroke
    - Abdominal Aortic Aneurysm
  - Respiratory problems

Tobacco Use

- What types of problems may occur?
  - Cancers
    - Lung, pancreatic, gastric
    - Bladder and kidney
    - Cervical and endometrial
  - Second-hand smoke
  - Problems with reduced fertility in women and low-birth weight babies, sudden infant death syndrome

Tobacco Use

- What types of problems may occur?
  - Cataracts
  - Candida infections of the mouth
  - Periodontitis
  - Plus……drug interactions

Tobacco Use

- Drug Interactions
  - Beta blockers – less effective for BP and HR lowering; additive peripheral vasoconstriction
  - Analgesics - ↓ analgesic effects in smokers; higher doses needed to achieve analgesia
  - Benzodiazepines - ↓ sedation and drowsiness (probably CNS stimulation)

Tobacco Use

- Drug Interactions
  - Antidepressants – plasma concentrations are lower (hence, they may be less effective)
  - Warfarin – tobacco has thrombogenic potential; harder for warfarin to work
  - Hormones, certain OCPs – thrombogenic potential

Tobacco Use

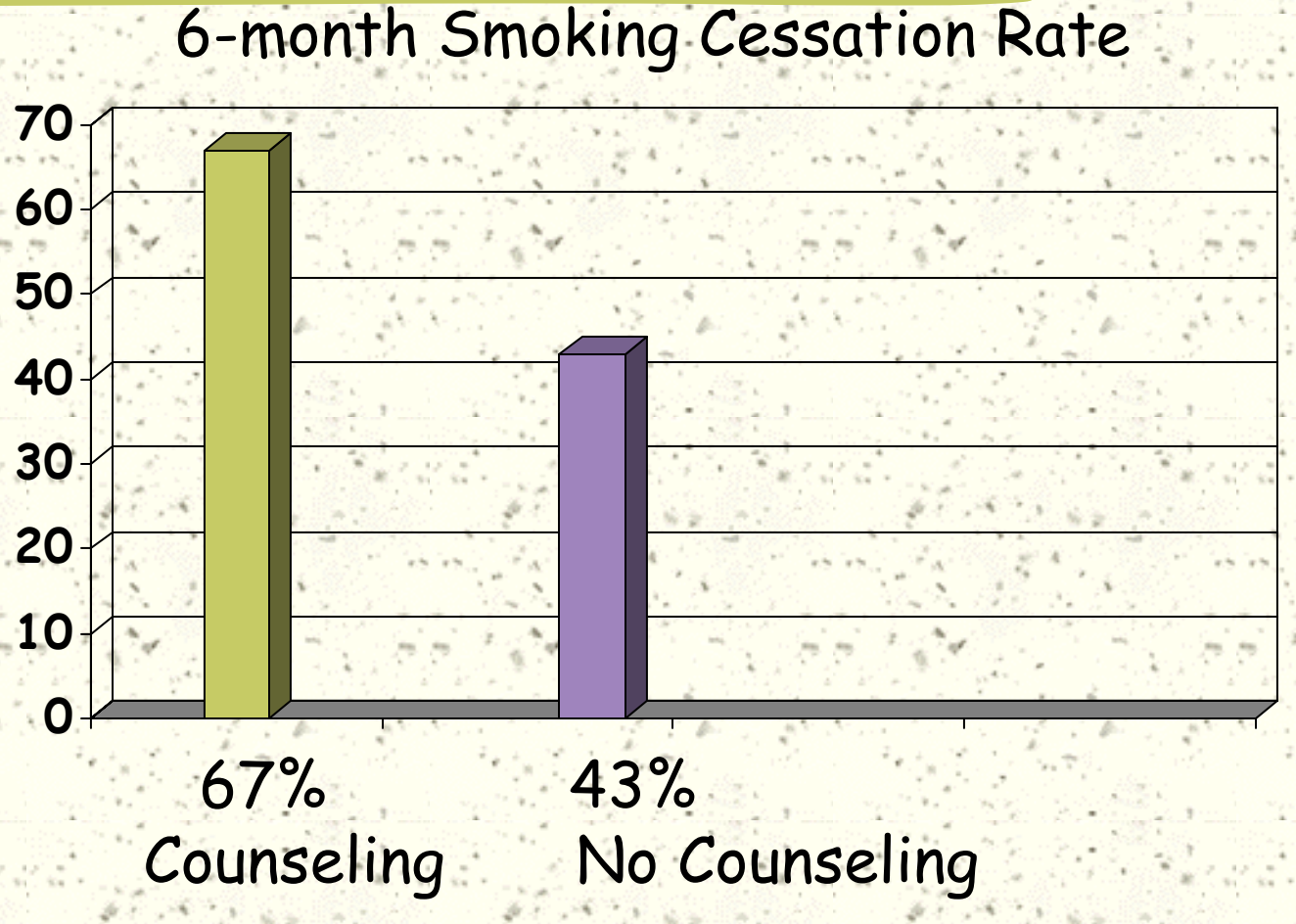
- Drug Interactions in patients with diabetes:
  - Tobacco causes cutaneous vasoconstriction
  - Insulin – Rate of absorption is affected by subcutaneous blood flow
    - 113% ↓ in extent of insulin absorption during cigarette smoking
    - 30% ↓ in extent of insulin absorption in the 30 minutes after smoking
  - Smokers may require more insulin compared to nonsmokers

Tobacco Use

- Disease Interactions in patients with diabetes:
  - Diabetes makes a person more predisposed to cardiac disease
    - A person with diabetes who smokes may have an even greater risk of cardiac disease
  - Tobacco users have peripheral vasoconstriction
    - Diabetes patients may also have ↓ peripheral blood flow and thus tobacco may exacerbate peripheral vascular disease

Does Smoking Cessation Counseling Work?

Does Smoking Cessation Counseling Work?



Dornelas EA, et al. Prev Med 2000;30:261-8

What Other Substances are Used for Coping?

- Marijuana
- Cocaine or crack
- Hallucinogens or psychedelics
- Heroin
- Amphetamines

Marijuana

- Used by 76% of current illicit drug users
- Similar to being intoxicated, thus may impair judgment and thus diabetes-related self-care behaviors
- Has been shown to acutely ↑ HR and BP

Marijuana

- Has been shown to cause hypoglycemia
  - Impaired judgment may mask symptoms of hypoglycemia
- Long-term excessive use may cause food cravings
  - Patients may gain weight and have ↑ in BG long term
- Drug interactions
  - With TCAs (pt may be taking for neuropathic pain) may see supraventricular arrhythmias, ↑ HR, confusion, short-term memory impairment, labile mood

Cocaine or Crack

- Used by 2.2 million Americans
- May impair judgment and thus diabetes-related self-care behaviors
- Powerful sympathomimetic
- May cause hyperglycemia via the sympathetic nervous system

Cocaine or Crack

- Strong vasoconstrictor
  - ↑ BP
  - May be related to MI
  - May be related to arrhythmia, sudden death
  - May cause stroke
  - May cause seizures
  - May be associated with bowel necrosis
  - May be associated with kidney failure

Hallucinogens or Psychedelics

- Include LSD, phencyclidine (PCP), or mescaline
- Used by 1.3 million Americans
- "Magic mushrooms" have not been shown to directly affect glucose metabolism
- One report indicated that long-term use is associated with mild kidney function decline
  - May be an issue in patients with DM
- Case report of ↑ flashbacks when used with sertraline

Heroin

- Used by 123,000 Americans
- In animals, heroin has shown ↑ insulin/glucagon release
  - Can this result in a drug interaction?
- Has been associated with several forms of kidney disease
  - Rhabdomyolysis (can this be ↑ when pt has DM and is on statins?)
  - May present as a nephrotic syndrome that may progress quickly to ESRD

Heroin

- Other problems reported
  - Hypotension
  - Hypoxia
  - Acidosis (predispose to DKA?)
  - Dehydration (predispose to DKA?)

Amphetamines

- May produce a counter-regulatory effect to insulin
  - Mediated via 5HT-stimulated catecholamine release
- May ↑ BP
- Drug interactions
  - Fluoxetine has ↑ SDC (inhibition of metabolism)
  - Serotonergic effects of fluoxetine may enhance dopaminergic actions
  - Hypertensive crisis with MAO Is

Study of Illicit Drug Use With Possible Implications For Patients With Diabetes

Kidney-Related Risks

- Study looked at harmful effect of illicit drug use on kidney function
- N=647 pts in VA Hypertension Clinic interviewed regarding illicit drug use (2.7% of users had DM; 76.1% on ACE Is)
- Followed up for median of 7 years to determine incidence of mild kidney function decline (↑ in Cr of ≥ 0.6 mg/dL)

Vupputuri S, et al: Am J Kidney Dis 2004;43:629-35

Kidney-Related Risks

- 23% of patients reported illicit drug use
  - 22.7% - marijuana
  - 9.3% - amphetamines
  - 6.7% - cocaine or crack
  - 4.3% - heroin
  - 3.1% - psychedelics

Vupputuri S, et al: Am J Kidney Dis 2004;43:629-35

Kidney-Related Risks

- Multivariate Adjusted Relative Risk for Mild Kidney Function Decline in Drug Versus Nondrug Users
  - Adjusted for age, race, education, income, smoking, alcohol consumption, SBP, use of BP meds, BMI, DM, dyslipidemia

Vupputuri S, et al: Am J Kidney Dis 2004;43:629-35

Kidney-Related Risks

- Multivariate Adjusted Relative Risk for Mild Kidney Function Decline in Drug Versus Nondrug Users

Any Drug	2.29 (1.04-5.06)*
Marijuana	1.96 (0.87-4.40)
Amphetamines	1.89 (0.41-8.68)
Cocaine or Crack	2.99 (1.12-8.04)*
Heroin	3.04 (0.83-11.07)
Psychedelics	3.92 (1.09-14.42)*

Vupputuri S, et al: Am J Kidney Dis 2004;43:629-35

Implications Of This Study

- Epidemiological evidence that illicit drug use may be associated with mild kidney function decline
- The association is particularly strong for cocaine and psychedelic drug use
- Illicit drug use may have a role in progression of chronic kidney disease
  - This should not be ignored as a risk factor for ESRD
  - Patients with DM may be especially vulnerable

Vupputuri S, et al: Am J Kidney Dis 2004;43:629-35

Studies of ETOH or Drug Use In Diabetes

ETOH/Drug Use in Teenagers with Diabetes (USA)

- Anonymous self-administered questionnaire
  - ETOH
    - 50% reported having tried alcohol
    - 25% reported ongoing use
  - Drugs of abuse
    - 25% reported having tried drugs of abuse
    - 5% reported ongoing use

Glasgow AM, et al: J Adolesc Health 1991; 12:11-14

Street Drug Use in Teenagers with Diabetes (UK)

- Anonymous confidential questionnaire
  - Street Drugs Used
    - Cannabis – 28.2%
    - Cocaine – 11.8%
    - Amphetamine – 8.2%
    - Ecstasy – 4.7%
    - Magic mushrooms – 3.5%
    - LSD – 2.4%
    - Solvents – 2.4%

Ng RSH, et al: Diabetic Medicine 2003; 21:295-6

Street Drug Use in Teenagers with Diabetes (UK)

- Anonymous confidential questionnaire
  - Epidemiology of Street Drugs Used
    - 29% admitted using street drugs
    - 80% of these reported using > once/month
    - 15.3% used more than one street drug
  - 72% not aware of adverse effects on diabetes

Ng RSH, et al: Diabetic Medicine 2003; 21:295-6

What About CAM Therapies?

What Other Substances are Used for Coping?

- Ginseng for energy?
  - Panax ginseng may ↑ BP
  - Panax ginseng may also ↑ SDCs of some drugs
  - American ginseng may benefit PPG
- St John's Wort for depression?
  - May induce metabolism of drugs that a person with diabetes it taking:
    - Angiotensin receptor blocker
    - Calcium channel blocker
    - OCPs
    - Cyclosporine
    - Many others

What Other Substances are Used for Coping?

- Valerian for sleep?
  - Probably OK, but watch for any ADRs
- Kava for anxiety?
  - May cause hepatotoxicity
- "Ephedrine-free" products for weight loss?
  - Bitter orange is an ephedrine analog and may produce cardiotoxicity

Conclusions

- HCPs need more education about substances that patients may be using to "cope"
- More research needs to be done in this area
- More education needs to be provided to patients about adverse effects of these substances
  - Patients should be cautioned to wear medic alert bracelets in case there are adverse events that occur
  - Patients should monitor BG before/after substance use

Questions